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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/517,774	10/13/2005	Didier Montarras	263955US0XPCT	6948

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EXAMINER	
LONG, SCOTT	

ART UNIT	PAPER NUMBER
1633	

NOTIFICATION DATE	DELIVERY MODE
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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Notice of the Office communication was sent electronically on above-indicated "Notification Date" to the following e-mail address(es):

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Office Action Summary	Application No.	Applicant(s)	
	10/517,774	MONTARRAS ET AL.	
	Examiner	Art Unit	
	Scott D. Long	1633	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *13 October 2005*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-12* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-12* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☒ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *3/2005*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Claim Status

Claims 1-12 are pending. Claims 1-12 are under current examination.

Oath/Declaration

The oath or declaration, having the signatures of all inventors, received on 13 October 2005 is in compliance with 37 CFR 1.63.

Information Disclosure Statement

The Information Disclosure Statements (IDS) filed on 8 March 2005 consisting of 1 sheets are in compliance with 37 CFR 1.97. Accordingly, examiner has considered the Information Disclosure Statements.

Priority

This application claims benefit as a 371 of PCT/FR03/02010 (filed 6/27/2003). The application also claims benefit from foreign application CANADA 2391638 (filed 6/28/2002). The instant application has been granted the benefit date, 28 June 2002, from the application CANADA 2391638.

Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 1-12 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. Claim 1 is directed to "a method for preparing...stem cells...comprising...maintaining of the cells obtained, in a specific culture medium...said method excluding cell culture." Since cell culture encompasses the concept of maintaining live cell lines separated from their original tissue source, which does not necessarily involve expansion of the cells, the examiner feels there is a contradiction in this claim. A skilled artisan might not understand how a method can comprise maintaining cell in culture while not culturing the cells. Perhaps the claim could be amended to recite, "said method excluding *in vitro* expansion and differentiation of said stem cells" in the last line of claim 1, or some language that more clearly approximates the teachings in the specification and does not create confusion for a skilled artisan attempting to avoid infringement. Clarificaiton is requested.

In addition, claim 2 contains unclear language, since the claim does not recite a, b, c, *and* d, it is also possible that Applicants meant to recite: a, b, c, *or* d. Clarification is required.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 1, 3-10 are rejected under 35 U.S.C. 102(b) as being anticipated by Okarma et al (US-6,143,508, issued 7 November 2000).

Claim 1 is directed to a method for preparing human or animal stem cells, said method comprising: cell extraction; mechanical dissociation; enzymatic dissociation; maintaining of the cells obtained, in a specific culture medium for preserving diversity and plasticity, said method excluding cell culture. Okarma et al. describe methods of preparing homogeneous populations of cells (abstract). Okarma et al. teach, "The cellular source may be any mixture of cells....Cellular sources of interest from animal hosts may include organs, such as blood, brain, kidney, spleen, heart, intestine, bone marrow" (col.4, lines 13-18). Okarma et al. teach, "Of particular interest are stem cells, which may be obtained from bone marrow or peripheral blood. These stem cells may serve as progenitors of one or more of the blood cell lineages" (col.8, lines 46-47). Okarma et al. further teach, "Where the cells are held together by a membranous or other connecting material, the cells may be dispersed either by mechanically or enzymatically in accordance with conventional techniques. The individual cells may then be dispersed in their appropriate nutrient medium for separation by the subject

method" (col.4, lines 25-30). Okarma et al. also teach, "These cells will then usually be concentrated by any convenient means to substantially remove the medium in which they have been isolated or maintained" (col.4, lines 40-49).

Claim 3 is directed to the method of claim 1 wherein said stem cells are animal or human stem cells selected form the group consisting of progenitor stem cells for a tissue. Okarma et al. teach, "The cellular source may be any mixture of cells....Cellular sources of interest from animal hosts may include organs, such as blood, brain, kidney, spleen, heart, intestine, bone marrow" (col.4, lines 13-18). Okarma et al. teach, "Of particular interest are stem cells, which may be obtained from bone marrow or peripheral blood. These stem cells may serve as progenitors of one or more of the blood cell lineages" (col.8, lines 46-47).

Claim 4 is directed to the method of claim 3, wherein the tissue is selected from the group consisting of skin, liver, heart, bone, and nerve tissues. Since the methods of Okarma et al. teach the isolation of stem cells and the sources of the cells can be brain, heart, bone, the examiner asserts that the limitations of claim 4 are taught by Okarma et al.

Claim 5 is directed to a medicinal product comprising the human or animal stem cells, obtained according to the method of claim 1, and one or more additives. Since the specification does not define "additives", the examiner contends that the cells in media or PBS, as taught by Okarma et al. meet the limitations of claim 5.

Claim 6 is directed to a stem cell obtained according to the method of claim 1. The examiner contends that the stem cells taught by Okarma et al. meet the limitations of claim 6.

Claim 7 is directed to a method of treatment comprising implanting autologous or heterologous animal stem cells, obtained according to the method of claim 1. Okarma et al. teach, "the bone marrow, depleted of the unwanted cells, is immediately prepared for transplantation into the marrow recipient." (col.3, lines 11-19).

Claim 8 is directed to a cell composition comprising human or animal stem cells, obtained according to the method of claim 1. The examiner contends that the stem cells taught by Okarma et al. meet the limitations of claim 8.

Claim 9 is directed to the composition of claim 8, wherein the stem cells have the ability to colonize and the Ability to allow function al recovery. Besides the fact, that the limitations of claim 9 to not alter the structure of the composition of claim 8, Okarma et al. teach, that their method can be used to isolate "transplanted cells from blood as an index of recovery from bone marrow transplantation." (col.3, lines 27-28).

Claim 10 is directed to a method of treating disease by cell therapy or gene therapy, comprising, injecting the human or animal stem cells, obtained by the method of claim 1, into a subject in need thereof. Okarma et al. teach "infusing" stem cells into patients.

Accordingly, Okarma et al. anticipated the instant claims.

Claims 1, 3-4, 6-9 are rejected under 35 U.S.C. 102(b) as being anticipated by Mignone et al. (WO2001/36482, published 25 May 2001).

Claim 1 is directed to a method for preparing human or animal stem cells, said method comprising: cell extraction; mechanical dissociation; enzymatic dissociation; maintaining of the cells obtained, in a specific culture medium for preserving diversity and plasticity, said method excluding cell culture.

Mignone et al. describe a method for transplanting neural stem cells, in which the cells are not precultured. (Mouse) brain tissue is placed in a specific medium (DMEM/F12) and dissociated, firstly by adding trypsin then by using mechanical means (pipette). The cells are collected by means of centrifugation, then stored in Hank's Buffered Salt Solution (HBSS) before being injected into a rat brain. After one week, it was possible to note the survival of the cells and their incorporation into the brain (page 1, lines 12-26; page 21, lines 22-27; example 8). Mignone et al. disclose all of the steps of the method of claim 1 and also meets the limitations of claims 3 and 4. The stem cells or cell compositions as well as the transplantation method disclosed in Mignone et al. meet the limitations of claims 6-9.

Accordingly, Mignone et al. anticipated the instant claims.

Claims 1, 3-9 are rejected under 35 U.S.C. 102(b) as being anticipated by DiMario et al. (Experimental Cell Research. 1995. Vol.216, No.2: 431-442).

Claim 1 is directed to a method for preparing human or animal stem cells, said method comprising: cell extraction; mechanical dissociation; enzymatic dissociation; maintaining of the cells obtained, in a specific culture medium for preserving diversity and plasticity, said method excluding cell culture.

DiMario et al. describe a method of myoblast transplantation, in which the cells are not precultured (i.e. – freshly prepared). (Chicken and quail) muscle tissue is placed in a specific medium (HBSS) and dissociated, firstly by using mechanical means (minced) and then by adding trypsin (page 432, col.1, last parag.). The cells were maintained in culture media containing horse serum, bFGF (differentiation inhibiting factor), are collected by means of filtration, then stored in Hank's Buffered Salt Solution (HBSS) before being injected into a chicken embryo hindlimb buds (page 433, col.1, Cell Transplantation). After several days, it was possible to note the survival of the cells and their incorporation into the hindlimbs (page 433, Results). DiMario et al. disclose all of the steps of the method of claim 1 and also meets the limitations of claims 3-5. The stem cells or cell compositions as well as the transplantation method disclosed in Mignone et al. meet the limitations of claims 6-9.

Accordingly, Mignone et al. anticipated the instant claims.

Claims 1, 3-9 are rejected under 35 U.S.C. 102(b) as being anticipated by Pouzet et al. (Circulation. 2000. Vol.102, No.19: III-210-III.215).

Claim 1 is directed to a method for preparing human or animal stem cells, said method comprising: cell extraction; mechanical dissociation; enzymatic dissociation; maintaining of the cells obtained, in a specific culture medium for preserving diversity and plasticity, said method excluding cell culture.

Pouzet et al. disclose a method for preparing skeletal myoblasts, in which the muscle tissue is chopped, then exposed to enzymatic dissociation. The cells are collected by means of sedimentation and centrifugation, then kept in a specific culture medium consisting of F12 with 20% FBS, and basic fibroblast growth factor (bFGF) (page III-211, Cell culture Methodology, col.1, last paragraph to col.2, line 4). These teachings meet the limitations of claims 1, 3-10.

Accordingly, Pouzet et al. anticipated the instant claims.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

Claims 1-12 are rejected under 35 U.S.C. 103(a) as being obvious over Pouzet et al. (Circulation. 2000. Vol.102, No.19: III-210-III.215) in view of DiMario et al. (Experimental Cell Research. 1995. Vol.216, No.2: 431-442).

The teachings of Pouzet et al. and DiMario et al. are recited above in the 35 USC § 102 section.

Both of these references teach the basic method claimed in the instant application.

Neither teach the exact limitations of claim 2, wherein the culture media comprises a) a nutritive medium; b) a protective factor; c) hormones; and d) differentiation inhibiting factors. However, both Pouzet and DiMario teach 3 of the 4 components of claim 2. Pouzet et al. teach medium consisting of F12 [nutritive medium] with 20% FBS [differentiation inhibiting factor], and basic fibroblast growth factor (bFGF) [differentiation inhibiting factor/hormone]. DiMario et al. teach culture media [nutritive medium] containing horse serum [differentiation inhibiting factor] and bFGF [differentiation inhibiting factor/hormone].

It would have been obvious to the person of ordinary skill in the art at the time of the invention was made to utilize medium containing a variety of hormones, differentiation inhibiting factors, and antioxidants, metabolism protectors, and metal protecting factors in the methods of Pouzet and DiMario.

It would have been obvious to the person of ordinary skill in the art at the time the invention was made to substitute commonly used tissue culture components such as ascorbic acid, N-acetylcysteine, anti caspases, L-carnitine, transferring, insulin, retinoic, acid, thyroid hormone, IGF-1, IGF2, FGFs, EGF, LIF, or serum in the method of Pouzet and DiMario.

The person of ordinary skill in the art would have been motivated to substitute one known, equivalent element for another to obtain predictable results. The claimed methods would have been obvious because the substitution of one known element for another would have yielded predictable results to one of ordinary skill in the art at the time of the invention. In the instant case, it would have been obvious to substitute any

of a variety of commonly used components used in culture medium in the invention of Pouzet and DiMario. For example, according to Sigma-Aldrich, Ascorbic acid (vitamin C) is an essential vitamin for the growth and maintenance of healthy cells *in vivo* and *in vitro*. Sigma-Aldrich also indicates, Ascorbic acid is an important water soluble anti-oxidant found in numerous media. Furthermore, Sigma-Aldrich sells L-carnitine from equine muscle and indicates on their website, that it occurs naturally in most mammalian tissue and is present in relative high concentrations of skeletal muscle and heart. As indicated in the teachings of Dimario, horse serum was used to supplement the medium; clearly this supplement would contain L-carnitine. So, while all of the 4 components of the specific culture medium of claim 2 are not explicitly taught, they were nevertheless present or would be obvious to include in standard culture medium. These were commonly known and used within the art of tissue culture for maintaining viability of cells.

Therefore the method as taught by Pouzet et al. in view of DiMario et al. would have been *prima facie* obvious over the method of the instant application.

Conclusion

No claims are allowed.

Examiner Contact Information

Any inquiry concerning this communication or earlier communications from the examiner should be directed to **Scott Long** whose telephone number is **571-272-9048**. The examiner can normally be reached on Monday - Friday, 9am - 5pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, **Joseph Woitach** can be reached on **571-272-0739**. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

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